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Award Number: DAMD17-97-C-7052

TITLE: Analytical and Characterization Studies of Organic
Chemicals, Drugs, and Drug Formulation

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REPORT DATE: July 2001

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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20020124 351

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 074-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503				
1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE July 2001	3. REPORT TYPE AND DATES COVERED Annual (1 Jul 00 - 30 Jun 01)		
4. Analytical and Characterization Studies of Organic Chemicals, Drugs, and Drug Formulation		5. FUNDING NUMBERS DAMD17-97-C-7052		
6. AUTHOR(S) Peter, Lim, Ph.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) SRI International Menlo Park, California 94025 E-Mail: lim@sri.com		8. PERFORMING ORGANIZATION REPORT NUMBER		
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		10. SPONSORING / MONITORING AGENCY REPORT NUMBER		
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited			12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 Words) During the annual contract period, 1 July 2000 to 30 June 2001, the project personnel continued to perform chemical/physical analyses on bulk pharmaceutical substances and formulated drug products of interest to the USAMRMC Drug Development Program for parasitic and infectious diseases, chemical and biological defense, etc. Specific objectives were to design, develop, validate, and apply methods to determine chemical and physical characteristics of bulk drugs, drug products, and to determine their stability under defined storage conditions. Special projects include verification of the absence of squalene in vaccine products.				
14. SUBJECT TERMS antiparasitic drugs, chemical defense agents, chemical analyses, stability studies			15. NUMBER OF PAGES 8	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

FOREWORD

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 N/A In conducting research using animals, the investigator(s) adhered to the "guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

 N/A For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal law 45 CFR 46.

 N/A In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institute of Health.

 N/A In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

_____In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.



PI – Signature

July 2001

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INTRODUCTION

This annual report for Contract DAMD17-97-C-7052 covers the period from 1 July 2000 to 30 June 2001. The report consists of a listing of the compounds/samples analyzed and a summary of the number of the types of studies performed. The report also includes a listing of personnel receiving pay from this effort and a bibliography of all publications and meeting abstracts that resulted from this contract.

This contract is concerned with the analytical, characterization, and stability studies of chemicals, drugs, and drug formulations. The studies are monitored by Mr. William Y. Ellis, the Contracting Officer Representative (COR), Chief, Department of Chemical Information, Division of Experimental Therapeutics, Walter Reed Army Institute of Research (WRAIR).

The overall objective of this project is the operation of an analytical laboratory to determine the identity, purity, strength, quality, physical and chemical properties, and stability of bulk pharmaceutical substances and formulated drug products of interest of the USAMRMC Drug Development Program for parasitic and infectious diseases, chemical and biological defense, anti-viral studies, etc. Specific objectives are to design, develop, validate, and execute methods to determine the following characteristics of candidate bulk pharmaceutical substances and formulated drugs:

- Identity, purity, and strength
- Stability
- Other physical and chemical characteristics, including weight variation, content uniformity, and other such compendial requirements
- Qualitative and quantitative identity of impurities
- Special projects not covered by the above headings.

ANNUAL REPORT (2000-2001)

Sample Analysis

During the contract period 1 July 2000 to 30 June 2001, analyses of the following samples were completed and the reports sent to the COR.

1. WR178460;BN78716, desbutylhalofantrine hydrochloride, bulk stability after 3.7 years storage at room temperature, Report No. 1027.
2. WR178460;BN78716, desbutylhalofantrine hydrochloride, bulk stability after 4.2 years storage at room temperature, Report No. 1032.
3. WR178460;BN78716, desbutylhalofantrine hydrochloride, bulk stability after 3.3 years storage at 35°C, Report No. 1025.
4. WR178460;BN78716, desbutylhalofantrine hydrochloride, bulk stability after 4.0 years storage at 35°C, Report No. 1034.
5. WR178460;BN78716, desbutylhalofantrine hydrochloride, bulk stability after 3.3 years storage at 50°C, Report No. 1026.
6. WR178460;BN78716, desbutylhalofantrine hydrochloride, bulk stability after 4.0 years storage at 50°C, Report No. 1035.
7. WR178460;BP18546, desbutylhalofantrine lactate, bulk assay, Report No. 1031.
8. WR242511;BM05816, 8-[(4-amino-1-methylbutyl)amino]-5-(1-hexyloxy)-6-methoxy-4-methylquinoline DL tartrate, bulk stability after 9 years storage at room temperature, Report No. 1018.
9. WR255663;BM04131, β -artelinic acid, bulk stability after 10 years storage at room temperature, Report No. 1020.
10. WR255663;BP12419 (Bottles A,B,C), β -artelinic acid, bulk drug assays, Report No. 1023.
11. WR255663;BP18322, β -artelinic acid, sodium salt, bulk drug assay, Report No.1024.
12. WR279396AH;BN64230, a cream formulation of paromomycin sulfate and gentamicin sulfate, stability after storage at 4°C for 40 months, Report No. 998.

13. WR279396;BP18359, Lot 00510100, a placebo ointment and WR279396:BP18340, Lot 00610100, paromomycin sulfate and gentamicin sulfate ointment, water determinations, Report No. 1019.
14. WR279396;BP18359, Lot 00510100, a placebo ointment and WR279396:BP18340, Lot 00610100, paromomycin sulfate and gentamicin sulfate ointment (second samples), moisture determination, Report No 1021.
15. WR282908;BP15036, Lot FAV041, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1006.
16. WR282908;BP15027, Lot FAV043, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1007.
17. WR282908;BP15045, Lot FAV044, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1008.
18. WR282908;BP15358, Lot FAV038, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1009.
19. WR282908;BP15376, Lot FAV037, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1010.
20. WR282908;BP15652, Lot FAV024, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1011.
21. WR282908;BP16024, Lot FAV031, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1012.
22. WR282908;BP17423, Lot FAV047, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1013.
23. WR282908;BP17432, Lot FAV048B, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1014.
24. WR282908;BP13989, Lot FAV008, anthrax vaccine adsorbed, verification of the absence of squalene in the titled vaccine product, Report No. 1033.

Special Projects

During this report period, we continued to devote a great deal of our time and effort to the determination of squalene in anthrax vaccine adsorbed products. Our initially developed and validated method has a lower limit of detection (LOD) of 70 ng squalene per 0.5-mL dose or 140 ppb; this is the method that has been applied to all of the anthrax vaccine adsorbed samples received through 2000. Owing to the need for a method of higher sensitivity, we have developed and validated a method that has a LOD of 1.8 ng squalene per 1.00 mL or 1.8 ppb. The

validation report for this newly developed method is Report No. 1029 and has been submitted to the COR. With this enhanced sensitivity, a 0.5-mL dose of anthrax vaccine that contains as little as 1.0 ng squalene can be readily detected and measured.

Publications and Presentations

A second draft of a publication entitled "Development and Application of an Analytical Method for the Determination of Squalene in Formulations of Anthrax Vaccine Adsorbed" has been submitted to the COR for approval for publication. A verbal approval for publication has been received.

Awards

No awards were received during the report period.

PERSONNEL

A listing of personnel who received major contract support during the report period is as follows:

Peter Lim, P.I.

Ronald Spanggord, Assistant P.I.

Meg Sun, Chemist

Patrick Macauley, Chemist

Laura Rasay, Chemist

SUMMARY/CONCLUSIONS

During the annual contract period, 1 July 2000 to 30 June 2001, 17 bulk drugs and stability study samples were analyzed for identity, purity, or stability. The absence of squalene was verified in 10 lots of anthrax vaccine adsorbed preparations.